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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,540	05/02/2002	Dan L. Eaton	P3230R1C001-168	1054

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EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,540	EATON ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/10/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence non compliance*.

DETAILED ACTION

1. Claims 1-6 are pending and under consideration. The claims are drawn to antibodies that bind to PRO1277 polypeptide of SEQ ID NO: 34.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.823(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.823 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.823 - 1.825). **Applicant is required to provide a paper copy of the CRF when filing the response to this Office Action.**

Information Disclosure Statement

4. The information disclosure statement, filed 9/10/2002, has been considered. The BLAST results demonstrate that applicants are aware of nucleic acids with identity/homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the Examiner cannot determine if said sequences constitute prior art.

Priority Determination

5. The claimed protein has no utility, see rejection below. Accordingly, priority is set at the instant filing date, 5/2/02.

Should the applicant disagree with the examiners factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to the date recited above which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of, and fully enabled for, prior to that date.

Rejections under 35 U.S.C. §101 and §112:

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The claims are directed to antibodies that bind the protein of SEQ ID NO: 34. The specification contains numerous asserted utilities for the claimed antibodies, including use to identify molecules that bind to PRO1277 (including agonists and antagonists), diagnostic assays, affinity purification, and for the therapeutic purposes. The utilities that pertain solely to nucleic acids (e.g. hybridization, chromosome and gene mapping, anti-sense) would not convey to

the encoded protein or the antibody. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO1277 protein, as each of the aforementioned utilities could be asserted for any naturally occurring protein, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO1277.

The specification asserts that PRO1277 is an unspecified secreted transmembrane polypeptide. However, this family of proteins does not possess a common utility, but rather the proteins that can be broadly classified and have different activities, that confer different uses on them. Accordingly, the mere identification of a protein as belonging to a family, while indicative of evolutionary relatedness, is not indicative of function, nor by extension, of utility. The structure of the putative PRO1277 peptide is briefly discussed in Figure 34, as having a signal peptide, corresponding to about amino acids 1-26, and putative transmembrane domains, corresponding to about amino acids 181-200. In addition, Applicants also describe potential N-glycosylation sites around amino acids 390-394 and 520-524. Further, potential N-myristoylation sites around amino acids 23-29, 93-99, 115-121, 262-268, 367-373, 389-395, 431-437, 466-472, 509-515, 570-576, 571-577, 575-581 and 627-633 have been described. Also described is a potential amidation site around amino acids 304-308. However, there is no functional characteristic associated with these motifs, hence the mere observation that they exist is not probative of function or utility. Further, there is no disclosure that the protein is expected to be a transmembrane protein, nor has any extracellular domain. There is no biological activity, expression

pattern, phenotype, disease or condition, ligand, binding partner, any other specific feature that is disclosed as being associated with PRO1277. Without any information as to the specific properties of PRO1277, the mere identification of such as having homology to a secreted transmembrane protein is not sufficient to impart any particular utility to the claimed antibodies.

The polynucleotide (cDNA) is disclosed to be more highly expressed in normal esophagus compared to the esophageal tumor based on the PCR amplification of cDNA libraries (see page 141). Similarly, it is also disclosed that the polynucleotide is also more highly expressed in normal skin compared to melanoma tumor (see page 141). Thus, the specification asserts that the polynucleotide encoding PRO1277 polypeptide being more highly expressed in normal esophagus vs. esophageal tumor and also normal skin vs. melanoma tumor renders the molecule useful for the diagnosis, as well as therapeutically as a target for the treatment (see page 140). There is no supporting evidence to indicate that the polypeptide encoded by the polynucleotide of the instant invention is more highly expressed in normal tissues compared to their tumor tissue counterparts, and as such one of skilled in the art would conclude that it is not supported by a substantial asserted utility or a well-established utility. Although, the specification claims that the polynucleotide is more highly expressed in normal esophagus and normal skin, the specification does not teach what is the normal level of expression, does not indicate how high the expression level is compared to for example, esophageal tumor or melanoma tumor; and does not provide a statistical correlation to the level of expression

(for example, there is no indication of how many samples were compared to study the expression). Furthermore, even if the tumor is malignant, the specification fails to describe the type or kind of tumor present in esophagus (for example, is it an adenocarcinoma etc.) and skin (for example, type of melanoma etc.). Without knowing the identity of the esophageal or melanoma tumor, one of skill in art cannot use the polynucleotides for diagnosis or therapeutic purposes as asserted. The specification does not disclose a correlation between any specific disorder and the altered level or form of the claimed polypeptides. Also, the specification does not predict whether the polypeptides would have high or low expression in a specific, diseased tissue (esophagus and skin) compared to the healthy tissue control. In addition, the specification does not teach or describe the function of this yet to identified polypeptide. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO1277 encoding polypeptides, as each of the aforementioned utilities could be asserted for any naturally occurring polypeptides, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO1277 polypeptides. In addition, since the specification states that the DNA was amplified from the cDNA library from different human tumor and human normal tissue samples, there is no possibility for direct comparison of the expression between the normal and tumor tissues (see page 140).

Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12: 82-88). The data presented in the specification were not corrected for aneuploidy. A slight

amplification of a gene does not necessarily mean overexpression in a tissue, but can merely be an indication that the cancer tissue is aneuploid. The preliminary data were not supported by analysis of mRNA or protein expression, for example. Also, the literature reports that it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased polypeptide expression, such that the claimed polypeptides would be useful for diagnosis of cancer or as a drug target. This fact is documented by Pennica et al. (1998, PNAS USA 95:14717-14722). In addition, they also observed that there was no correlation between WISP-2 mRNA expression and colon tumors. Furthermore they disclose that:

> "An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors." Therefore, data pertaining to PRO1277 nucleic acids do not necessarily indicate

any substantial utility regarding the claimed PRO1277 polypeptides or the antibodies binding to the polypeptide. Thus, the data does not support the implicit assertion that the nucleotide encoding PRO1277 can be used in cancer diagnosis or therapy. Significant further research would have been required of the skilled artisan to determine why PRO1277 is more highly expressed in normal tissue compared to tumor tissue to the extent that it could be used as a cancer diagnostic, and thus the implicitly asserted utility is not substantial.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed the polypeptides. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ: at 696.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8a. Claim 1 states that the claimed antibody "binds" the protein of SEQ ID NO: 34, whereas dependent claim 6 states that the antibody "specifically binds". The term "specifically" in claim 6 is a relative term that renders the claim indefinite. The term "specifically" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Further, the antibodies would presumably be of no use if they did not bind to the protein of SEQ ID NO: 34 with specificity; therefore, it must be presumed that there is some level of specificity implicit in all the claims. As the difference between "binds" and "specifically binds" cannot be determined, the metes and bounds of all the claims are unclear. Change of "specifically" would be remedial, but then claim 6 would be duplicate of claim 1.

Claim Rejections - 35 USC § 103

Priority is set at the instant filing date, 5/2/2002, as no disclosure to which priority is claimed meets the requirements of 35 U.S.C 101 and 112, first paragraph.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9a. Claims 1, 2 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sulston et al., Accession No: Q9UDNO or AAF19243, 21 December 1999 in view of Jacobs et al. (U.S. Patent No: 5 965 397).

Sulston et al. describes an amino acid sequence that has a 100% overall identity to SEQ ID NO: 34 (see Appendix A and B). However, Sulston et al. reference does not teach antibodies that bind to polypeptide of SEQ ID NO: 34 (see Appendix A).

Jacobs et al. et al. describes monoclonal antibodies capable of binding secreted protein (column 41, lines 50-60). Therefore, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was

made to generate antibodies as taught by Jacobs et al. using the polypeptide described in Sulston et al. that is identical to SEQ ID NO: 34 of the instant invention. The person of ordinary skill in the art would have been motivated to generate antibodies directed to the polypeptide described by Sulston et al. because this will allow one of skilled in the art to use the antibodies for immunodetection or therapeutic or diagnostic purposes. There is a reasonable expectation of success because generating various antibodies for purification, expression studies and therapeutic purposes is routine in the art. Therefore, the claims 1, 2 and 6 are rejected as obvious over Sulston et al., Accession No: Q9UDNO or AAF19243, 21 December 1999 in view of Jacobs et al. (U.S. Patent No: 5 965 397).

10. No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system.

Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

JS/06/04

Notice to Comply	Application No. 10/063,540	Applicant(s) Eaton et al.
	Examiner J. Schwadron	Art Unit 1647

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☑ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
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